

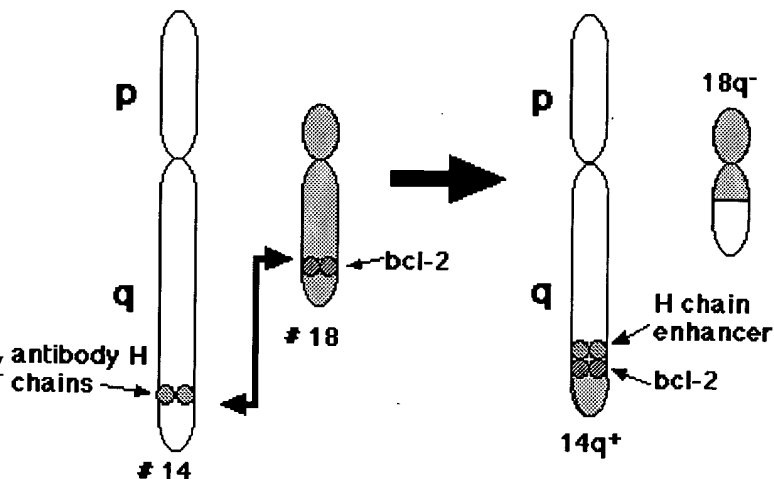
BCL-2

BCL-2 is a human proto-oncogene located on chromosome 18.

Its product is an integral membrane protein (called Bcl-2) located in the membranes of the endoplasmic reticulum (ER), nuclear envelope, and in the outer membranes of the mitochondria.

The gene was discovered as the translocated locus in a **B-cell leukemia** (hence the name). This translocation is also found in some B-cell lymphomas.

In the cancerous **B cells**, the portion of chromosome 18 containing the BCL-2 locus has undergone a reciprocal translocation with the portion of chromosome 14 containing the antibody heavy chain locus. This t(14;18) translocation places the BCL-2 gene close to the heavy chain gene enhancer.



This enhancer is very active in B cells (whose job it is to synthesize large amounts of antibody). So it is not surprising to find that the Bcl-2 protein is expressed at high levels in these t(14;18) cells.

What makes BCL-2 a proto-oncogene?

B cells, like all activated lymphocytes, die a few days after they have had a chance to do their job. This ensures that they do not linger around after the threat has been dealt with and turn their attack against self components. Aging B cells kill themselves by apoptosis.

But high levels of the Bcl-2 protein protect the cells from early death by apoptosis. The Bcl-2 protein suppresses apoptosis by preventing the activation of the caspases that carry out the process [Discussion].

So genes encoding inhibitors of apoptosis must be added to the list of genes that can act as oncogenes. In this case the effect is not achieved by increasing the rate of cell proliferation but by reducing the rate of cell death.

The antibody gene loci are dangerous places for proto-oncogenes to take up residence. Translocation of the proto-oncogene **c-myc** close to the enhancer of the antibody heavy chain genes also produces cancerous B cells resulting in Burkitt's Lymphoma.

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